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| 10/570,909      | 03/29/2006  | Carsten Hopf         | 50125/147001        | 1220             |

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BOSTON, MA 02110

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| EXAMINER |
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HILL, KEVIN KAI

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| ART UNIT | PAPER NUMBER |
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1633

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| NOTIFICATION DATE | DELIVERY MODE |
|-------------------|---------------|

07/09/2009

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentadministrator@clarkelbing.com

|                              |                                      |                                      |  |
|------------------------------|--------------------------------------|--------------------------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b><br>10/570,909 | <b>Applicant(s)</b><br>HOPF, CARSTEN |  |
|                              | <b>Examiner</b><br>KEVIN K. HILL     | <b>Art Unit</b><br>1633              |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 7-10 and 69-71 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 7-10 and 69-71 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

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**Detailed Action**  
***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 14, 2009 has been entered.

***Election/Restrictions***

Applicant had elected with traverse the invention of Group I, claim(s) 7-11, drawn to a method for identifying a gamma-secretase and/or a beta secretase modulator, and a method for preparing a pharmaceutical composition for the treatment of neurodegenerative diseases, wherein the agent that modulates a gamma-secretase.

***Amendments***

Applicant's response and amendments, filed April 14, 2009, to the prior Office Action is acknowledged. Applicant has cancelled Claims 1-6 and 11-68, and amended Claims 7 and 10. Applicant's new claims have been entered into the application as requested and will be examined on the merits herein, as they are considered to belong to the elected group.

Claims 7-10 and 69-71 are under consideration.

***Priority***

This application is a 371 of PCT/EP04/09771, filed September 2, 2004. Acknowledgment is made of Applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Certified copies of the following foreign applications have been provided:

EPO 03019642.2, filed September 5, 2003,  
PCT/EP2003/013980, filed December 10, 2003,  
EPO 04001895.4, filed January 29, 2004,  
EPO 04001894.7, filed January 29, 2004,  
EPO 04007447.8, filed March 26, 2004,  
PCT/EP2004/004891, filed May 7, 2004,  
PCT/EP2004/004889, filed May 7, 2004, and  
EPO 04018874.0, filed August 9, 2004.

Accordingly, the effective priority date of the instant application is granted as September 5, 2003.

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### ***Examiner's Note***

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment will not be reiterated. The arguments in the April 14, 2009 response will be addressed to the extent that they apply to current rejection(s).

### ***Specification***

#### ***Sequence compliance***

37 CFR 1.821(d) states: "[w]here the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing" in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO:" in the text of the description of claims, even if the sequence is also embedded in the text or the description or claims of the patent application.

1. **The disclosure is objected to for the following reason:** this application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences are set forth in the specification that lack sequence identifiers.

Applicant's attention is drawn, in particular, to the following locations in the instant specification: pg 18, ¶4 and pg 377, ¶2.

Applicants are required to comply with all of the requirements of 37 CFR 1.821 - 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive.

37 CFR 1.821(f) states that in addition to the paper copy required by paragraph (c) of this section and the computer readable form required by paragraph (e) of this section, a statement that the content of the paper and computer readable copies are the same must be submitted with the computer readable form, *e.g.*, a statement that "the information recorded in computer readable form is identical to the written sequence listing."

Note that if the SEQ.txt file was received via EFSWeb and the text file meets the requirements for the paper copy and CRF, no statement is required.

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The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the examination of the application on the merits, the results of which are communicated below.

### ***Claim Objections***

2. **Claim 8 is objected to** under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is advised that should claim 7 be found allowable, claim 8 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

The claim is dependent upon step (a) of claim 7, and recites that the test compound is brought into contact with FADS2 and the interaction of FADS2 with the test compound is determined. However, Claim 7, step (a), recites the step of determining whether a given test compound binds to FADS2. Thus, the test compound is necessarily brought into contact with FADS2 and the interaction of FADS2 with the test compound is determined in Claim 7, step (a). While claim 8 is worded differently than claim 7, step (a), the active step(s) is/are the same, and thus claim 8 is a substantial duplicate of claim 7, step (a).

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. **The prior rejection of Claims 7-10 under 35 U.S.C. 112, second paragraph, is withdrawn** in light of Applicant's amendment to Claim 7 to clarify the inventive method steps.

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4. **The prior rejection of Claims 7-10 under 35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement **is withdrawn** in light of Applicant's amendments to the claims limiting the invention to a method to identify a gamma secretase inhibitor.

5. **The prior rejection of Claims 7-10 are rejected under 35 U.S.C. 112, first paragraph**, as failing to comply with the enablement requirement **is withdrawn** in light of Applicant's argument that, for example, the screening may be performed by contacting compounds making up the library with FADS2 immobilized on a solid phase, and harvesting those library members that bind to the protein (well known in the art as "panning" techniques), which the Examiner finds persuasive.

6. **Claims 7-10 and 69-71 are rejected under 35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. As discussed in the Interview Summary, paper mailed March 31, 2009, "the Examiners noted that the test compound that binds to FADS2 (Claim 7(a)), as presently claimed, may result in no change in FADS2 activity, increased FADS2 activity or decreased FADS2 activity; however, the instant specification appears to only support decreased FADS2 activity that consequently inhibits gamma secretase activity and thereby inhibits A $\beta$ -42 formation (e.g. pgs 3, 37, 49, 365 and 378)."

In response to the Interview Summary, Applicant has amended the claim to recite that the compound is capable of **modulating** [emphasis added]  $\gamma$ -secretase activity to reduce A $\beta$ -42 formation, thereby identifying an inhibitor of A $\beta$ -42 formation. At issue is that the term 'modulating' (Claim 7, line 6), reasonably embracing compounds that activate or inhibit  $\gamma$ -secretase activity. Again, the specification only supports decreased FADS2 activity that consequently inhibits  $\gamma$ -secretase activity and thereby inhibits A $\beta$ -42 formation. At the time of the invention, Marlow et al (BBRC 305:502-5509, 2003) taught that increasing the expression of  $\gamma$ -secretase component proteins increased  $\gamma$ -secretase activity, resulting in increased production

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of A $\beta$ -42. Conversely, blocking expression of any one of these proteins using RNAi (much like the working examples disclosed in the instant specification) will destabilize the other subunits and consequently result in a loss of  $\gamma$ -secretase activity (pg 503, col. 1, ¶1; pg 506, col.s 1-2, joining ¶). Similarly, Takahashi et al (J. Biol. Chem. 278(20):18664-18670, 2003) taught that a compound that reduces the generation of A $\beta$ -42 does so by inhibiting  $\gamma$ -secretase activity. Accordingly, a person of ordinary skill in the art would not view the Applicant to have been in possession of the full scope of the claimed invention, specifically the activation of FADS2 to activate  $\gamma$ -secretase activity, the activation of FADS2 to inhibit  $\gamma$ -secretase activity, or the inhibition of FADS2 to activate  $\gamma$ -secretase activity, and thereby inhibit A $\beta$ -42 formation.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 103***

7. **The prior rejection of Claims 7-10 under 35 U.S.C. 103(a)** as being unpatentable over Fechteler et al (WO 01/49871 A2, July 12, 2001; \*of record) in view of Winther et al (WO 01/70993 A2, September 27, 2001; \*of record), Conquer et al (Lipids 35(12):1305-1312, 2000) and Nakada et al (NeuroReport 1:153-155, 1990) **is withdrawn** in light of the cited prior art failing to provide a sufficient nexus teaching that FADS2 plays a functional role in the processing of APP by gamma secretase.

8. **The prior rejection of Claims 69-71 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Fechteler et al (WO 01/49871 A2, July 12, 2001; \*of record) in view of Winther et al (WO 01/70993 A2, September 27, 2001; \*of record), Conquer et al (Lipids 35(12):1305-1312, 2000) and Nakada et al (NeuroReport 1:153-155, 1990), as applied to claims 7-10 above, and in further view of Cho et al (J. Biol. Chem. 274:471-477, 1999; complete search results for SEQ ID NO:76 are available in SCORE) **is withdrawn** for reasons discussed above.

### ***Conclusion***

9. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to KEVIN K. HILL whose telephone number is (571)272-8036.

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The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill/

Examiner, Art Unit 1633